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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/774,181	04/26/2001	Bernhard A. Sabel	202306US0PCT	8612

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OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
OH, SIMON J	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/774,181	Applicant(s) SABEL ET AL.	
	Examiner Simon J. Oh	Art Unit 1615	

-- The MAILING DATE of this communication app ars on th cov r she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Papers Received

Receipt is acknowledged of applicant's amendment and response, received on 10 February 2003.

Claim Rejections - 35 USC § 112

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim 47 contains the trademarks/trade names GENAPOL™ and BAUKI™. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe stabilizer/surfactant and, accordingly, the identification/description is indefinite.

The examiner recommends simply removing all mention of the aforementioned trademarks/trade names in the claim and amending it to list the claimed stabilizers/surfactants intended to be encompassed by the use of the trademarks/trade names solely in terms of the

formulae that the applicant has used to define substances of the GENAPOL™ and BAUKI™ series.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 11 and 15-34 have been cancelled.

Claims 35-44 and 46-54 are rejected under 35 U.S.C. 102(b) as being anticipated by Kreuter *et al.*

The Kreuter *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material and a drug that is absorbed, adsorbed, or incorporated within the nanoparticles themselves. The nanoparticles are also coated with at least one surfactant, which allows for the delivery of drugs across the blood-brain barrier. Suitable carriers for the nanoparticles include buffers or other physiologically acceptable carrier solution. The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm, and may be delivered orally, intravenously, or intramuscularly to mammals, including humans. The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system, including tumor tissue. Such substances that

may be used include diagnostic agents (See Summary of the Invention, Pages 6-7; and Page 11, 2nd Paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 11, 4th Paragraph). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 13, Lines 8-10). Specific types of polymers suitable for use in the composition include polyacetates, polystyrenes, polyvinyls, polyacrolein, gelatin, albumin, polysaccharides, and polyglutaraldehyde (See Page 9, 2nd Paragraph). Specific types of surfactants suitable for use in the composition include polaxamers, polysorbates, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols, ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series (See Page 10). The use of dextran 70,000 as a stabilizer is disclosed (See Pages 14-15, Examples 1 and 2).

Claims 35-44 and 46-54 are rejected under 35 U.S.C. 102(a) as being anticipated by Sabel *et al.*

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

The Sabel *et al.* document discloses a nanoparticle composition that allows the delivery of drugs across the blood-brain barrier. The composition comprises a polymeric material; a drug that is adsorbed or incorporated within the nanoparticles; and at least one stabilizer, which allows for the delivery of drugs across the blood-brain barrier (See Summary of the Invention, Pages 5-9). Suitable carriers for the nanoparticles include water and physiologically acceptable carrier solutions containing salts and/or buffers (See Page 17, 2nd Paragraph; and Page 20, Line 23 to Page 21, Line 7). The nanoparticles possess a diameter ranging from 1 nm to 1,000 nm (See Page 11, Lines 1-2), and may be delivered orally, intravenously, or intramuscularly to mammals, including humans (See Page 22, Line 21 to Page 23, Line 12). The drugs that may be used with the nanoparticle composition include those substances that affect or act on the nervous system, including tumor tissue (See Page 12, middle paragraph). More specific examples of suitable drugs include chemotherapeutic agents; anti-cancer drugs; and hormones and hormone antagonists (See Page 13). Specific types of anti-cancer drugs listed include alkylating agents, antimetabolites, nitrogen mustards, ethylenamines, methylmelamines, alkylsulfonates, folic acid analogs, pyrimidine analogs, purine analogs, vinca alkaloids, and antibiotics (See Page 15, Lines 1-3). Specific types of polymers suitable for use in the composition include polystyrenes, polyacrylates, polyvinyls, polyacrolein, polyglutaraldehyde, polysaccharides, gelatin, and albumin (See Page 18, Lines 1-6). Specific types of stabilizers suitable for use in the composition include polaxamers, polysorbates, sodium stearate, sodium lauryl sulfate, metal salts of fatty acids, metal salts of fatty alcohol sulfates, ethoxylated phenols, ethoxylated diphenols, ethoxylated triglycerides, glycerol monostearate and surfactants of the Genapol™ and Bauki™ series. Specific surfactants disclosed include polysorbate 85, polysorbate 81, and dextran 12,000

(See Page 16, 3rd Paragraph). See also Pages 27-35, Claims 1-5, 7, 9, 11-16, 18, 20, 22, 23, 27, 29-33, and 36-40.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 35-54 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kreuter *et al.* in view of Sabel *et al.* and Stainmesse *et al.*

The relevant portions of Kreuter *et al.* and Sabel *et al.* are detailed in the rejections of Claims 35-44 and 46-54 under 35 U.S.C. 102(b) and 35 U.S.C. 102(a), respectively.

Neither the Kreuter *et al.* nor the Sabel *et al.* document discloses of a nanoparticle composition comprising doxorubicin or mitoxantrone as a drug.

The Stainmesse *et al.* patent teaches a nanoparticle formulation and a method for its preparation (See Abstract). The nanoparticles are preferably less than 500 nm in diameter and an active substance in a polymer matrix. The examples of suitable polymer material include gelatin, polylactic acid, and copolymers of acrylic acid, acrylates, and acrylic acid polymers (See Column 2, Line 27 to Column 3, Line 45). Examples are given where nanoparticles comprising doxorubicin as the drug and Polaxamer 188 as the surfactant (See Column 5-7, Examples 1, 6, and 7). A process of preparing a suspension of the nanoparticles in a solution sodium chloride is disclosed, as well as the administration of such nanoparticles by intravascular injection (See Column 9, Line 41 to Column 10, Line 8).

It would be obvious to one of ordinary skill in the art to combine the teachings of Kreuter *et al.*, Sabel *et al.*, and Stainmesse *et al.* into the objects of the instant application. One of ordinary skill would be motivated to do so, because as stated in *In re Kerkhoven*, 205 USPQ 1069, 1072 (CCPA- 1980), "It is prima facie obvious to combine two compositions, each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition which is to be used for the very same purpose." As this court explained in Crockett, 126 USPQ 186, 188 (CCPA- 1960), the idea of combining them flows logically from their having been individually taught in the prior art. In the instant case, all three references teach nanoparticle compositions that comprise a polymer material, a drug, and a stabilzer or surfactant. Regarding the claim limitations drawn to a method treating cancer, and more particularly brain cancer, the critical feature of the inventions disclosed in Kreuter *et al.* and Sabel *et al.* of the delivery of a drug across the blood-brain barrier, along with the disclosure of the use of anti-cancer drugs in the nanoparticle composition makes such treatment methods obvious to one of ordinary skill in the art. Thus, the claimed invention as a whole is *prima facie* obvious.

Response to Arguments

Applicant's arguments filed 10 February 2003 have been fully considered but they are not persuasive.

Regarding the response to the rejections under 35 U.S.C. 102 from the previous office action, it is the position of the examiner that in the base generic claims, the instantly claimed mechanism by which the applicant treats brain cancer has failed to establish the avoidance of

anticipation by the prior art. It is immediately apparent to one of ordinary skill in the art that by the administration of the same general category of drug in the same manner, using the same composition, one would be able to treat the same disease.

Regarding the response to the rejection under 35 U.S.C. 103 from the previous office action, respectfully disagrees with the applicants' arguments. In the response filed on 10 February 2003, the applicants have relied upon a narrower definition of the term "blood-brain barrier" in order to argue against the obviation of the instantly claimed invention by the prior art. In analyzing the patentability of the claims, the examiner must give both the prior art and the claims in their present form their broadest reasonable interpretation. See MPEP § 2111 and 2123.

Furthermore, in determining the obviousness of claims in view of the prior art, it has been established that the genus, in this case, the central nervous system, renders obvious the species, in this case, the brain. See MPEP § 2144.08. The applicant has not shown that the instantly claimed invention possesses specificity with respect to the treatment of brain cancer.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Simon J. Oh whose telephone number is (703) 305-3265. The examiner can normally be reached on M-F 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on (703) 308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Simon J. Oh
Examiner
Art Unit 1615

sjo
March 12, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600